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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/256,156	02/24/1999	STEPHEN GILLIES	LEX-003	9492

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EXAMINER

MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 07/29/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Applicati n N .

09/256,156

Applicant(s)

GILLIES ET AL.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-24, 26 and 27 is/are pending in the application.
- 4a) Of the above claim(s) 14-24 and 26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-13 and 27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Continued Prosecution Application***

The request filed on 11/16/2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09256156 is acceptable and a CPA has been established. An action on the CPA follows.

### ***Formal Matters***

Claims 1-4, 6-24 and 26-27 are pending. Claims 14-24 and 26 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 1-4, 6-13 and 27 are under consideration.

### ***Claim Rejections - 35 USC § 112 first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide support for the invention as now claimed: an antibody-based fusion protein which has a longer circulating half-life in vivo than an antibody-based fusion protein comprising a portion of an IgG1 CH2 domain linked to said non-Ig protein.

Applicant's amendment, Paper No. 14, 2/28/2001, does not provide sufficient direction for the written description for the above mentioned limitations of claims 2 and 27. The

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specification originally discloses an antibody-based fusion protein with enhanced in vivo circulating half-life obtained by linking as least the CH2 domain of IgG2 or IgG4 to a second non-immunoglobulin protein (page 3, lines 25-27). The specification as filed does not provide a written description or set forth the metes and bounds of the phrase: an antibody-based fusion protein which has a longer circulating half-life in vivo than an antibody-based fusion protein comprising a portion of an IgG1 CH2 domain linked to said non-Ig protein. The specification does not provide direction for the instant antibody-based fusion protein encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above.

***Claim Rejections - 35 USC § 102***

Claims 1, 3, 6-9, 13 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hoogenboom et al. (1991), for reasons of record set forth in Paper No. 12, 8/29/2000.

Hoogenboom et al. teaches the design and production of two antibody-TNF fusion proteins (page 1031, Figure 1 and page 1032, Figure 2). In one antibody-TNF fusion construct, the human TNF gene is linked to the CH2 domain of the human gamma-1 chain. In this construct Leu-235 was deleted, thus decreasing binding of the antibody-TNF fusion protein to Fc receptors (page 1029, column 2, second paragraph). Thus, the limitations of claims 1, 3, 6-9, 13 and 25 are met.

Applicant argues that since the antibody fusion construct taught in Hoogenboom contains only 3 amino acids of the CH2 domain, it does not meet all the limitations of the instant claims. However, claim 1 reads "at least a portion of a CH2 domain". The three amino acids of the CH2 domain comprise a portion of a CH2 domain, and thus the claim limitations are met, and the claims anticipated.

***Claim Rejections - 35 USC § 103***

Claims 1, 3, 6-9, 13, 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoogenboom et al. (1991), in view of U.S. Patent No. 6,100,387.

The teaching of Hoogenboom et al. has been set forth, above. Hoogenboom et al. does not disclose an antibody based-fusion protein which comprises the CH2 domain of an IgG4 constant region. U.S. Patent No. 6,100,387 (column 20, lines 22-25) discloses the construction and expression of a chemokine-encoding fragment, a fragment containing a linker and part of the

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Fc portion of the IgG4 gene, a fragment containing the rest of the Fc portion of the IgG4 gene, and a vector fragment. The Fc region of this chimeric gene encodes a protein which is comprised of the hinge, CH2, and CH3 regions of human IgG4. Therefore, it would have been obvious to one of skill in the art at the time the invention was made to produce an antibody-based fusion protein with an Fc region comprising the CH2 domain of IgG4. The motivation is provided in U.S. Patent No. 6,100,387 (column 24, Table 2 and 3) which shows the success of these antibody-based fusion polypeptides to bind to receptors expressed by several human cell lines.

Applicant argues that neither the Hoogenboom reference nor the '387 patent teaches, suggests or motivates their combination to obtain the fusion protein of claim 27. However, the previous Office action set forth the teaching of Hoogenboom which is an antibody-TNF fusion construct, the human TNF gene is linked to the CH2 domain of the human gamma-1 chain. The '387 patent discloses the construction and expression of a chemokine-encoding fragment, a fragment containing a linker and part of the Fc portion of the IgG4 gene. The motivation is provided in U.S. Patent No. 6,100,387 (column 24, Table 2 and 3) which shows the success of these antibody-based fusion polypeptides to bind to receptors expressed by several human cell lines. Therefore, the Examiner has established that it would be prima facie obvious to one of skill in the art to combine the antibody-based chemokine fusion protein of Hoogenboom with an IgG4 CH2 domain as disclosed in the '387 patent, and the rejection is maintained.

Claims 1, 4, 7-8, 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoogenboom et al. (1991) in view of WO 97/30089.

The teaching of Hoogenboom et al. has been set forth, above. Hoogenboom et al. does not disclose an antibody based-fusion protein which comprises the CH2 domain of an IgG3 heavy chain which comprises a mutations or deletions at Leu235. WO 97/30089 discloses the construction, synthesis and expression of an IL-2/antibody fusion protein (page 9, first paragraph). This fusion protein has the N-terminus of human IL-2 fused to the C-terminus of IgG3, including the CH2 domain (page 10, third paragraph). This IL-2/antibody fusion protein has an increased half-life (page 10, fourth paragraph). WO 97/30089 also discloses that the antibody may be fused to a lymphokine including, *inter alia*, GM-CSF (page 6, paragraph 2). WO 97/30089 teaches that the IgG3-IL-2 fusion binds the FcγRI with slightly lower affinity than that of IgG3 alone (page 10, third paragraph). Thus it would have been obvious to one of skill in the art at the time the invention was made to produce an antibody based-fusion protein which comprises the CH2 domain of an IgG3 heavy chain which comprises a mutations or deletions at Leu-235. The motivation and expectation of success is provided in WO 97/30089 which teaches that fusing IL-2 to an IgG3 has an increased half-life.

### ***Conclusion***

No claim is allowed.

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***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.  
Patent Examiner  
Art Unit 1646  
July 18, 2002



DAVID S. ROMEO  
PRIMARY EXAMINER